

# Vessel wall damage by X-rays and 15 MeV neutrons. An experimental study.

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## SUMMARY

During the last two decades there has been a great interest in the application of fast neutrons and other types of densely ionizing radiation in radiotherapy and radiobiology.

This thesis describes the results of a comparative experimental study on the atheromatous changes of elastic arteries due to irradiation with 200 kVp X-rays and 15 MeV neutrons.

The investigation is the continuation of a series of earlier experiments, in which examination of the effect of X-irradiation on several mucopolysaccharide systems, including the arterial wall, resulted in the hypothesis that the radiation-induced atheromatous changes of the vessel wall are primarily caused by depolymerization of the mucopolysaccharide ground substance.

These experiments, as well as vessel wall damage described in the literature, either found in the autopsy material of irradiated patients, or induced by experimental irradiation of laboratory animals, are briefly summarized.

A number of radiobiological concepts, such as Linear Energy Transfer (LET), absorbed radiation dose, Relative Biological Effectiveness (RBE) and Oxygen Enhancement Ratio (OER) are discussed.

One chapter deals with the methods applied for neutron dosimetry: the activation method, the scintillation method and the ionization method.

In two simple mucopolysaccharide systems, synovial fluid and subcutaneous connective tissue membranes, the degrading effect of X-rays and neutrons is compared. Due to the depolymerization of the mucopolysaccharides the viscosity of synovial fluid decreases and the permeability of the connective tissue membranes for saline increases after irradiation. In both systems a RBE of 0.6 has been found for fast neutrons.

The atheromatous changes in the wall of elastic arteries (lipid penetration into the vessel wall and the formation of plaques consisting of large, lipid-filled foam cells) are studied in the carotid arteries of hypercholesterolemic rabbits, two months after irradiating the arteries with different doses of X-rays or neutrons. On account of the RBE of 0.6, mentioned earlier, and the hypothesis for radiation-induced atheromatosis, the RBE of fast neutrons for the atherogenic effect was expected to be smaller

than 1. However, the plaque formation and lipid penetration due to 500, 1000 and 2000 rad of X-rays correspond to the effects of 250, 500 and 1000 rad of neutrons respectively, resulting in a RBE of about 2 of 15 MeV neutrons for the atherogenic effect. This result is not in accordance with the hypothesis mentioned above, but gives strong evidence that mainly a cellular mechanism participates in the pathogenesis of radiation-induced atheromatosis.

With electron-microscopic observations the development of the atheromatous lesions has been studied from a few hours after irradiation up to several weeks later. As early as 8h following irradiation mononuclear cells appear in the subendothelial space of the vessel wall, presumably monocytes from the blood. In hypercholesterolemic animals more and more lipid-containing vacuoles appear in these monocytes, until they have gradually transformed into foam cells, visible from the second day following irradiation.

Smooth muscle cells migrating from the medial layer through the fenestrae of the lamina elastica interna into the subendothelial space, also showing an increasing number of lipid-vacuoles, constitute a second cell type participating in the process of plaque formation. Smooth muscle cells in the media sometimes show lipid-containing vacuoles as well.

The discussion of the obtained results contains a short description of theories known from the literature about the pathogenesis of the atheromatous plaque. Due to differences between the human clinical situation and the laboratory-animal situation extrapolation of the results to man is difficult. With this restriction the conclusion of the investigation is that in therapeutic irradiation with X-rays as well as with fast neutrons severe damage to blood vessels in the irradiated area has to be taken into account as an unwanted side-effect, particularly in patients with a high serum cholesterol level. Comparable damage must be expected for neutron and for X-ray irradiation.